Oral and Monoclonal Antibody Treatments for Relapsing Forms of Multiple Sclerosis: Effectiveness and Value

Public Meeting — January 20, 2023

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

AN ICER PROGRAM
NEW ENGLAND CEPAC
COMPARATIVE EFFECTIVENESS PUBLIC ADVISORY COUNCIL

Clinical and Patient Experts

Bruce A. Cohen, MD, Professor of Neurology, Northwestern University Feinberg School of Medicine

- *Dr. Cohen has equity interests in Abbott Laboratories, AbbVie, and CVS Health. He also served as a site PI for the OPERA trial of ocrelizumab funded by Northwestern University.*

Annette Langer-Gould, MD, PhD, Regional Lead for Translational Neuroscience, Southern California Permanente Medical Group; MS Specialist, Los Angeles Medical Center

- *Dr. Langer-Gould served as the site PI for ocrelizumab in the relapsing-remitting Phase III trial. Dr. Langer-Gould also served as the Assistant Medical Director at Genentech from September 2006 – September 2007, where she oversaw the rituximab and ocrelizumab development programs.*

Lauren Hirschfeld, Person Living with MS; District Activist Leader, National MS Society

- *No conflicts of interest to disclose.*

Bari Talente, JD, President, MS Coalition; Executive Vice President of Advocacy and Healthcare Access, National MS Society

- *No conflicts of interest to disclose.*

Why Are We Here Today?

I’ve felt hostage to MS my whole life. People see that I’m “well” and don’t understand what I’m actually going through. My treatments help but they’re an expensive hassle that I have to budget for every year. Treatment costs take the place of vacations, a new car, dining out. As healthy as I may look, MS is a ball and chain.

Person Living with MS

Why Are We Here Today?

- What happens the day these treatments receive FDA approval?
- Questions about:
  - What are the risks and benefits?
  - How do new treatments fit into the evolving landscape?
  - What are reasonable prices and costs to patients, the health system, and the government?
  - What lessons are being learned to guide our actions in the future?

The Impact on Rising Health Care Costs for Everyone

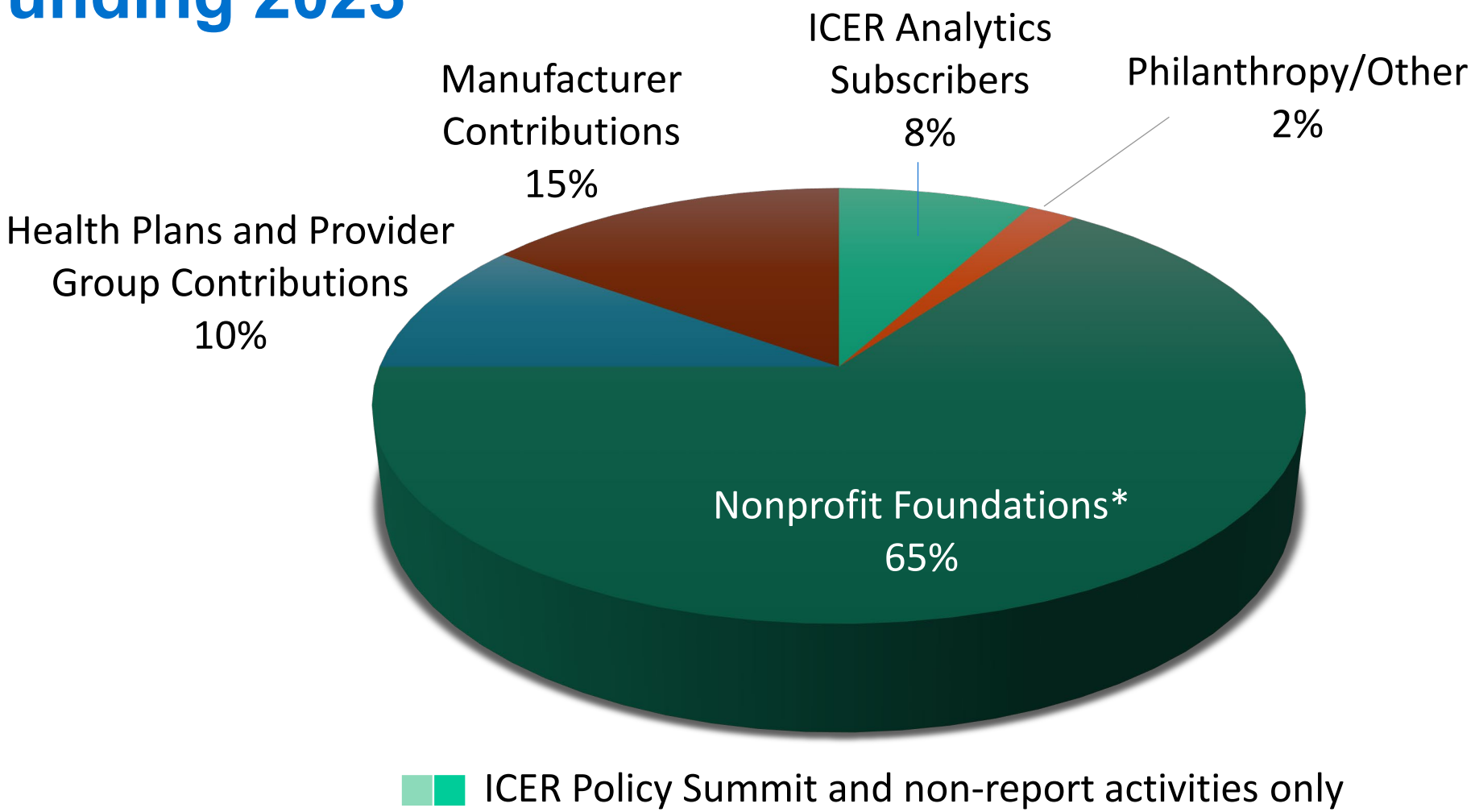
https://khn.org/news/article/diagnosis-debt-investigation-100-million-americans-hidden-medical-debt/

ICER

Organizational Overview

- New England Comparative Effectiveness Public Advisory Council (CEPAC)
- Institute for Clinical and Economic Review (ICER)

Funding 2023



How Was the ICER Report Developed?

- Scoping with guidance from patients, clinical experts, manufacturers, and other stakeholders
- Internal ICER evidence analysis and cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - Bruce A. Cohen, Professor of Neurology, Northwestern University Feinberg School of Medicine
  - Annette Langer-Gould, MD, PhD, MS Specialist, LA Medical Center
  - Simone Huygens, Visiting Fellow, Erasmus School of Health Policy and Management
  - Matthijs Versteegh, PhD, MA, BSc, Director, Institute for MTA, Erasmus University of Rotterdam
  - Bari Talente, JD, President, MS Coalition; EVP, Advocacy and Healthcare Access, National MS Society
  - Lisbeth Finseth, MS, Senior Manager of Advocacy, National MS Society
  - Elisabeth Oehrlein, PhD, MS, Consultant, MS Coalition
- How is the evidence report structured to support CEPAC voting and policy discussion?

Value Assessment Framework: Long-Term Value for Money

Agenda

Time (ET)	Activity
10:00 am—10:20 am	**Meeting Convened and Opening Remarks** Steven D. Pearson, MD, MSc, ICER
10:20 am—11:00 am	**Presentation of the Clinical Evidence** Grace A. Lin, MD, ICER
11:00 am—11:40 am	**Presentation of the Economic Model** Melanie D. Whittington, PhD, MS, ICER
11:40 am —12:00 pm	**Public Comments and Discussion**
12:00 pm—12:45 pm	**Lunch Break**
12:45 pm—1:45 pm	**New England CEPAC Vote on Clinical Effectiveness and Value**
1:45 pm—2:00 pm	**Break**
2:00 pm—3:30 pm	**Policy Roundtable**
3:30 pm—4:00 pm	**Reflections from New England CEPAC**
4:00 pm	**Meeting Adjourned**

Presentation of the Clinical Evidence

Grace A. Lin, MD

Medical Director, Health Technology Assessment, ICER

Professor of Medicine and Health Policy, University of California, San Francisco

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Key Collaborators

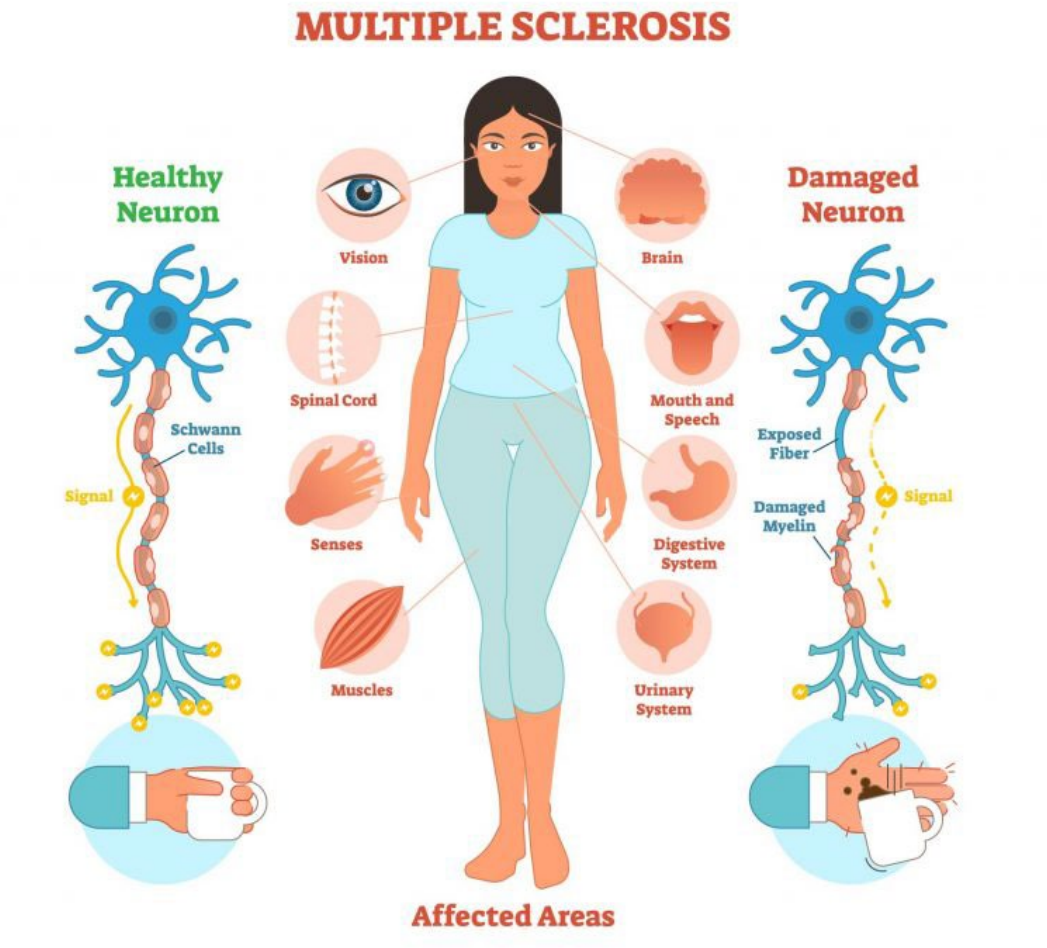
- **Dmitriy Nikitin, MSPH**, Research Lead, Evidence Synthesis, ICER
- **Serina Herron-Smith**, Associate Research Manager, ICER
- **Avery McKenna**, Senior Research Assistant, Evidence Synthesis, ICER
- **Foluso Agboola, MBBS, MPH**, Vice President of Research, ICER

Disclosures:

- Grace A. Lin received funding from ICER for this report.

Background: Multiple Sclerosis

- Autoimmune disorder of the central nervous system affecting almost 1 million Americans
- Diagnosis: Often in young adulthood (20-30s) and female predominance (3:1)
- Total annual economic burden of MS in the US: ~$85 billion; direct medical costs >$63 billion
- Multiple organ systems affected



Insights from Discussions with Patients

- Symptoms of MS impact physical and emotional health, work, education, family planning, and social/leisure activities
  - Many symptoms are “invisible” and are a challenge to manage in daily life
- Economic impact of MS: Lost wages from missed work, transition to part-time work, high out-of-pocket costs for medications and equipment
- Treatment
  - Main goals of treatment are to preserve function and remain as independent as possible, may need both disease-modifying and symptomatic medications
  - Treatment options and shared decision-making are important
  - Loss of ambulation should not lead to less aggressive treatment

Standard of Care and Management

- Comprehensive treatment of MS also includes both DMTs and supportive care such as:
  - Symptomatic medications
  - Psychological support
  - Management of comorbidities
  - Lifestyle interventions and rehabilitation
- Uncertainty surrounding ideal therapeutic approach for DMT
  - Escalation: Start with moderate efficacy DMT with more tolerable safety profile
  - Induction: Start with high efficacy DMT but higher risk of serious adverse effects

Scope of Review

- Compare clinical effectiveness and safety of oral and monoclonal antibody DMTs for the treatment of adult patients with **relapsing forms of MS**
  - RRMS: Periodic relapses with complete or near recovery
  - SPMS: Progressive worsening of neurologic activity following RRMS
- Focus of review: First-line therapies and new clinical evidence since ICER's 2017 MS Class Review
  - Specific focus on newest DMT, ublituximab

Interventions and Comparators

- Intervention: Ublituximab (Briumvi®)
- Comparators: Oral and monoclonal antibody DMTs
  - S1P receptor modulators: Fingolimod (Gilenya®), ozanimod (Zeposia®), siponimod (Mayzent®), ponesimod (Ponvory®)
  - Fumarates: Dimethyl fumarate (Tecfidera®), monomethyl fumarate (Bafiertam®), diroximel fumarate (Vumerity®)
  - Teriflunomide (Aubagio®)
  - Anti-CD20: ocrelizumab (Ocrevus®), ofatumumab (Kesimpta®), rituximab (Rituxan®)
  - Natalizumab (Tysabri®)

Interventions and Comparators

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  - Anti-CD20: ocrelizumab (Ocrevus®), ofatumumab (Kesimpta®), rituximab (Rituxan®)
  - Natalizumab (Tysabri®)

Key Clinical Outcomes

- Annualized relapse rate: Per-person average number of relapses in one year
- Confirmed disability progression at 3 and 6 months (CDP-3/6): Worsening of neurologic deficits measured by changes in Expanded Disability Status Scale (EDSS)
- MRI outcomes, including total and new T1/T2 lesions
- Patient-centered outcomes: Confirmed disability improvement (CDI), MS Functional Composite, MS Quality of Life, SF-36

Clinical Evidence

Ublituximab vs. Teriflunomide

	ULTIMATE I	ULTIMATE II
Outcomes	**N=545**	**N=544**
ARR, RR (95% CI)	0.41 (0.27, 0.62)	0.51 (0.33, 0.78)
CDP-6, HR (95% CI)	0.66 (0.36, 1.21)	
NEDA, OR (95% CI)	5.44 (3.54, 8.38)	7.95 (4.92, 12.84)

ARR: annualized relapse rate, CDP: confirmed disability progression at 6 months, NEDA: no evidence of disease activity, HR: hazard ratio, OR: odds ratio, RR: rate ratio

Ublituximab vs. Teriflunomide

- MRI outcomes
  - Mean number of gadolinium+ T1 Lesions significantly lower in ublituximab groups (RR 0.03; 95% CI 0.02, 0.06)
  - Similar results were observed for new or enlarging T2 lesions

- Quality of life
  - Improvements in the MS Quality of Life-54 and SF-36 at week 96 favored ublituximab in all subcomponents

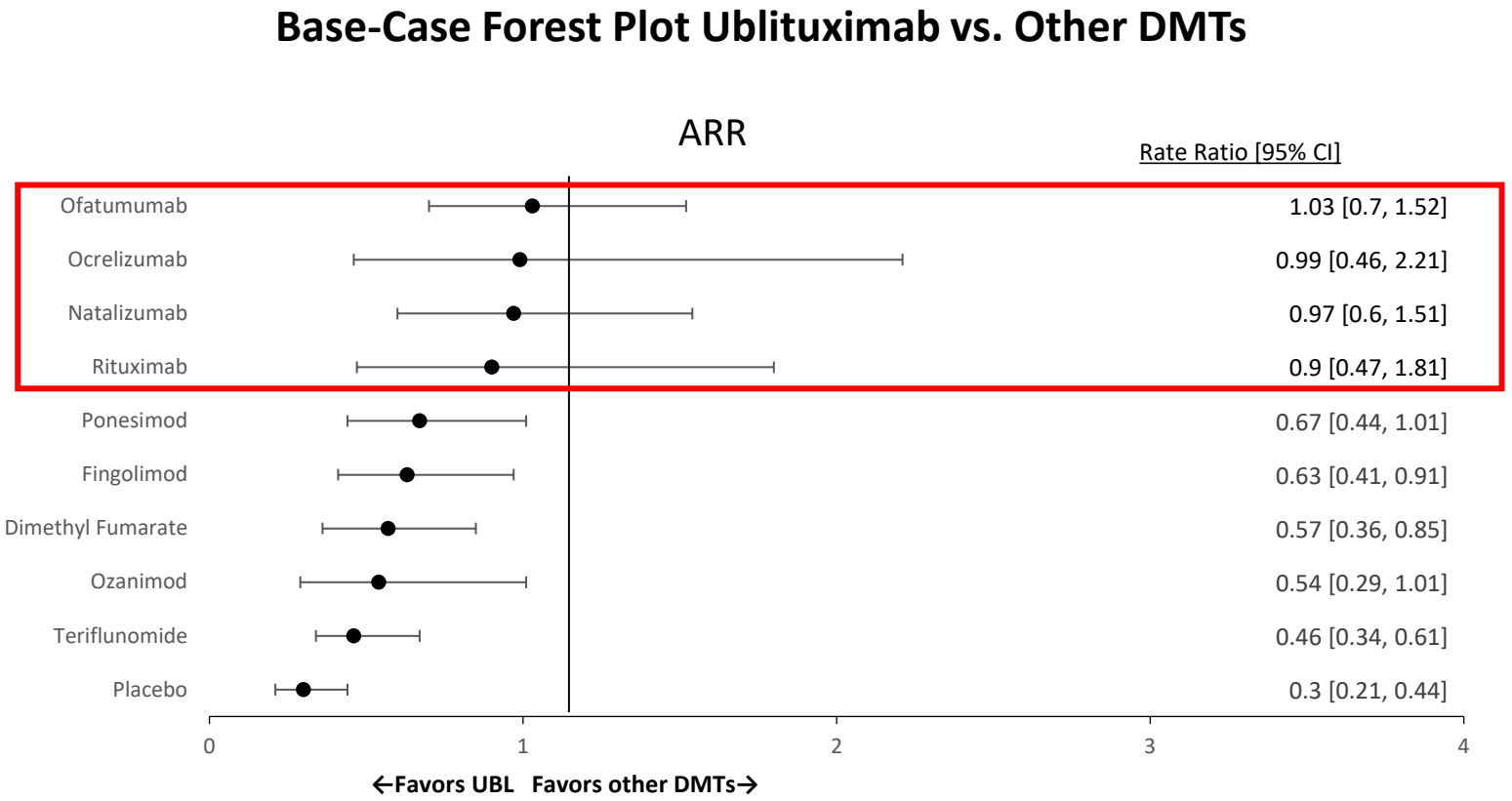
Network Meta-Analysis Methods

- Outcomes: Annualized relapse rate, confirmed disability progression (3 and 6 months)
- Bayesian Markov Chain Monte Carlo method
- Base case: Random-effects model
- Sensitivity analyses: Fixed-effects model, exclusion of older interferon trials

NMA Key Baseline Characteristics

- Trials ranged in size (104-1,133) and duration (48-120 weeks)
- Primarily younger, female, White population with RRMS
- Active disease
  - Baseline relapses in past 12 months: 1-1.5
  - Baseline EDSS: 1.6-3
- Variable prior DMT use (2-74%)

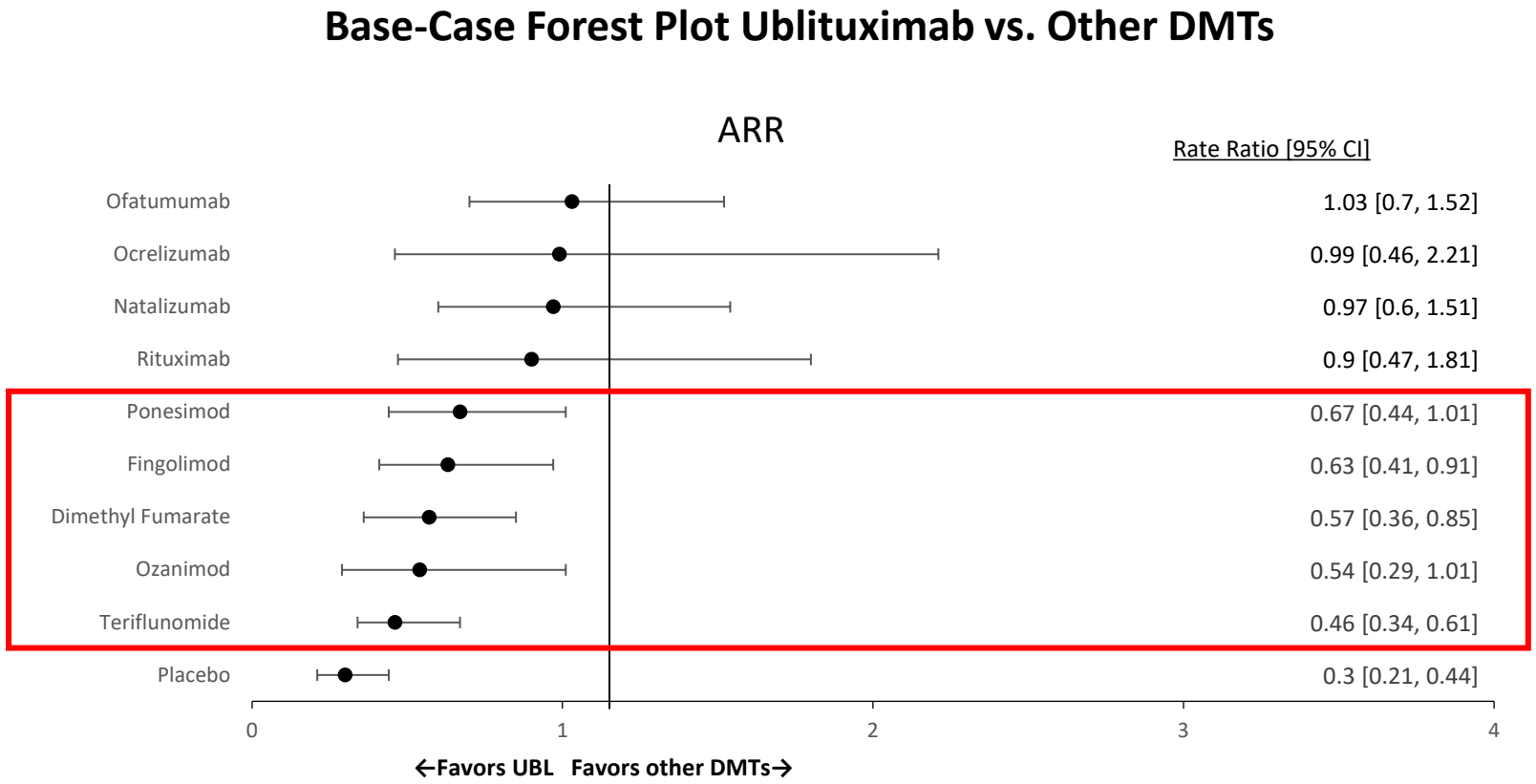
NMA Results: Annualized Relapse Rate



ARR: annualized relapse rate, CI: credible interval, DMT: disease-modifying therapy, PBO: placebo

Monoclonal antibodies are highlighted with a red box.

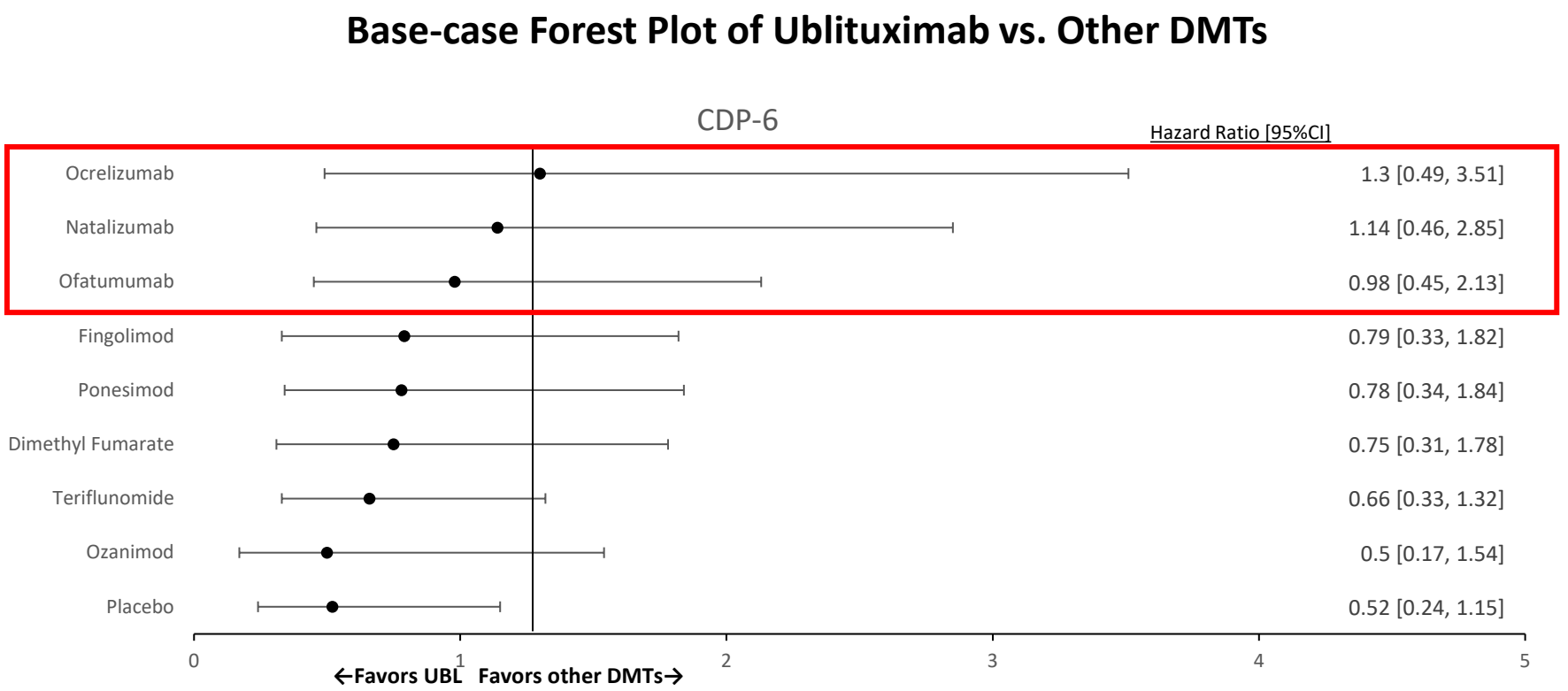
NMA Results: Annualized Relapse Rate



ARR: annualized relapse rate, CI: credible interval, DMT: disease-modifying therapy, PBO: placebo

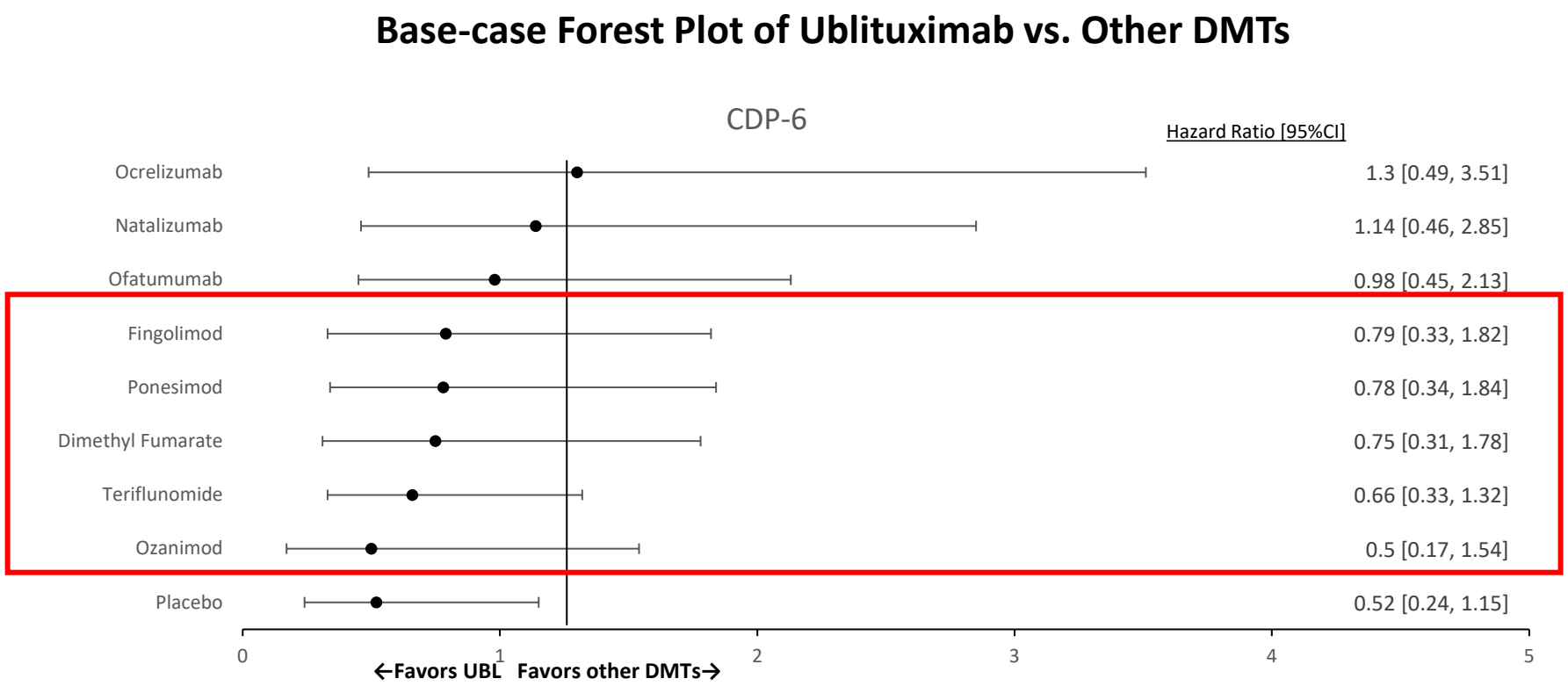
Oral therapies are highlighted with a red box.

NMA Results: 6 Month CDP



CD6: confirmed disability progression sustained for 6 months, CI: credible interval, DMT: disease-modifying therapy, PBO: placebo
Monoclonal antibodies are highlighted with a red box.

NMA Results: 6 Month CDP



CD6: confirmed disability progression sustained for 6 months, CI: credible interval, DMT: disease-modifying therapy, PBO: placebo
Oral therapies are highlighted with a red box.

MRI Outcomes

- Outcomes not measured consistently across trials so unable to include in NMA to compare DMTs
- All DMTs reduced either total number of or new lesions on MRI or both
- Monoclonal antibodies appear to be slightly more effective than oral medications

Patient-Centered Outcomes

- Cognitive function, fatigue, mobility, and quality of life measures are important to patients but were not consistently measured across trials
- MS Functional Composite: Measure of mobility and cognitive function
  - Statistical difference over comparator found in ublituximab and fingolimod RCTs
- CDI is emerging trial outcome of restorative function
  - Greater number of ublituximab patients showed improvement in disability vs. teriflunomide (CDI-6 9.6% vs. 5.1%; HR: 2.03; 95% CI: 1.27, 3.25)

Harms – Ublituximab

- Infusion reactions and upper respiratory tract infections were most common in RCTs
- Greater incidence of serious adverse events (10.8% vs. 7.3%) and discontinuation due to adverse effects (4.2% vs. 0.7%) vs. teriflunomide
- Prior to first dose: Hepatitis B virus screening and quantitative serum immunoglobulin screening

Harms

- Monoclonal antibodies
  - Increased risk of infection due to B-cell depletion
  - Infusion and injection-related reactions
  - **Black box warnings:** Progressive multifocal leukoencephalopathy in natalizumab and rituximab (seen in non-MS indications)
- Oral therapies
  - Fumarates: Flushing and gastrointestinal events
  - S1P receptor modulators: First dose monitoring due to cardiac concerns
  - Teriflunomide: Hepatotoxicity and embryofetal toxicity black box warning

Controversies and Uncertainties

- Lack of long-term efficacy and safety data for ublituximab
- Off-label use of rituximab for MS
- Lack of head-to-head data amongst and between classes
- Trial heterogeneity may affect NMA results
- Patient-important outcomes not well measured across clinical trials

Potential Other Benefits and Contextual Considerations

- MS is a chronic disease, impact is large over the lifespan
  - Impact on education, work, and family planning
  - Caregiver impact progressively increases due to loss of mobility
- Treatment burden is large but may be less with oral treatments and IV infusions
- Black Americans with MS may experience poorer outcomes
- COVID-19: Delays in receiving care and impact on person's response to vaccines while on B-cell depleting therapies

Public Comments Received

- Other trials should be considered for inclusion into NMA network
- Rituximab should not be included in review due to lack of FDA label for MS
- Consider other patient-relevant outcomes outside of NMA
- Consider long-term, real-world evidence where available for DMTs

Summary

- All DMTs are effective in reducing relapses; ublituximab appears similar to other monoclonal antibodies and better than oral DMTs and placebo
- Impact on disease progression is less certain, but ublituximab and the monoclonal antibodies may be slightly more effective than oral DMTs
- Harms differ across drugs and classes
- Ongoing trials will help answer questions about treatment sequence and discontinuation

ICER Evidence Ratings

Treatment	Comparator	Evidence Rating
Adults with RRMS		
Ublituximab	Natalizumab	I: Insufficient
	Ofatumumab	I: Insufficient
	Ocrelizumab	I: Insufficient
	Rituximab	I: Insufficient
	Fumarate class (dimethyl, diroximel, monomethyl)	C++: Comparable or better
	Fingolimod	C++: Comparable or better
	Ozanimod	C++: Comparable or better
	Ponesimod	C++: Comparable or better
	Siponimod	I: Insufficient
	Teriflunomide	B: Incremental
	Placebo/no DMT	A: Superior

DMT: disease-modifying therapy, RRMS: relapsing-remitting multiple sclerosis

Questions

Presentation of the Economic Model

Melanie D. Whittington, PhD

Director of Health Economics

Institute for Clinical and Economic Review

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Disclosures

No conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care manufacturers or insurers.

Objective

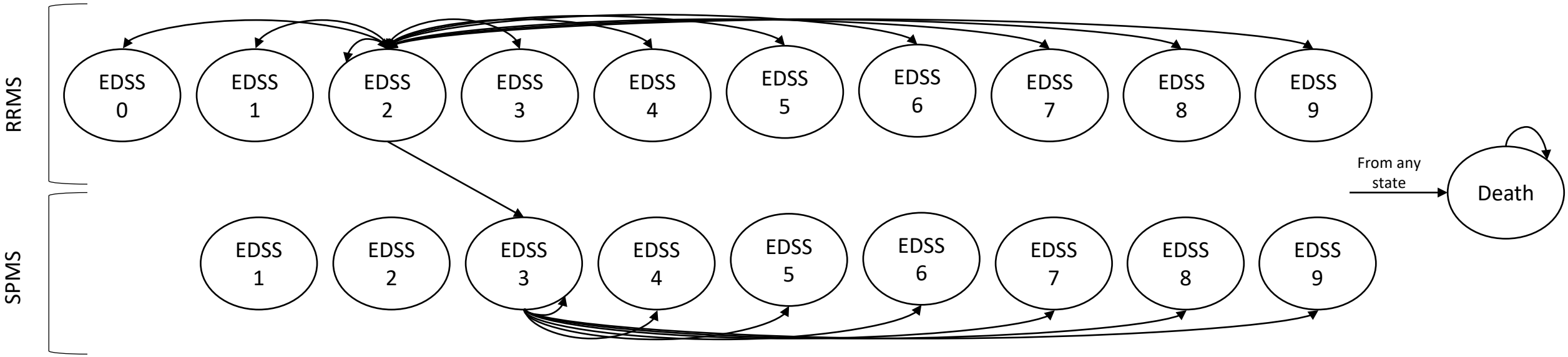
- To estimate the lifetime cost effectiveness of monoclonal antibody treatments for the treatment of relapsing forms of MS
- Interventions
  - Ublituximab (Briumvi®, TG Therapeutics)
  - Natalizumab (Tysabri®, Biogen)
  - Ofatumumab (Kesimpta®, Novartis)
  - Ocrelizumab (Ocrevus®, Genentech)
- Comparator: Dimethyl fumarate (generic)

Methods in Brief

Methods Overview

- **Model**: Markov
- **Setting**: US
- **Perspective**: Health care sector (base case), modified societal
- **Time Horizon**: Lifetime
- **Discount Rate**: 3% per year (costs and outcomes)
- **Cycle Length**: 1 year
- **Primary Outcomes**: Cost, QALYs, evLYs, life years, years without ambulatory restrictions, years without a wheelchair

Model Schematic



A relapse can occur in any health state.

Arrows are only depicted for one health state within RRMS and one health state within SPMS.

Population

- Adults ages 18 years and older in the US with relapsing forms of MS

Baseline Characteristic	Value
Mean Age at Baseline	38 years
Percent Female	68%
Percent EDSS 0 at Baseline	4%
Percent EDSS 1 at Baseline	23%
Percent EDSS 2 at Baseline	30%
Percent EDSS 3 at Baseline	23%
Percent EDSS 4 at Baseline	14%
Percent EDSS 5 at Baseline	6%

EDSS: Expanded Disability Severity Scale

Key Model Assumptions

- Trial-reported discontinuation was annualized and applied over the first 2 years
  - Discontinuation after 2 years was assumed to be related to serious adverse events and did not vary by treatment
- Upon discontinuation, patients transitioned to a subsequent treatment with cost and effectiveness similar to market leading monoclonal antibody
- Separate from modeled discontinuation, the cohort remained on treatment over the lifetime time horizon

Key Model Inputs: Treatment Efficacy

DMT	Relative Risk of Disease Progression	Rate Ratio for Relapse Rate
Ublituximab	0.53	0.30
Natalizumab	0.46	0.31
Ofatumumab	0.54	0.29
Ocrelizumab	0.41	0.30
Dimethyl Fumarate	0.70	0.53

DMT: disease-modifying therapy

Key Model Inputs: Annual Treatment Discontinuation

	Ublituximab	Natalizumab	Ofatumumab	Ocrelizumab	Dimethyl Fumarate
Years 1 and 2	3.9%	2.5%	4.9%	4.7%	8.8%
Years 3+	1.5%				

Key Model Inputs: Utilities

EDSS State	Utility, RRMS	Utility, SPMS
0	0.8752	N/A
1	0.8342	0.7905
2	0.7802	0.7365
3	0.6946	0.6509
4	0.6253	0.5816
5	0.5442	0.5005
6	0.4555	0.4118
7	0.3437	0.3000
8	0.2433	0.2095
9	0.1267	0.1034

EDSS: Expanded Disability Status Scale, RRMS: relapsing-remitting multiple sclerosis, SPMS: secondary progressive multiple sclerosis

Key Model Inputs: Health State Costs

EDSS State	Annual MS Direct Costs	Annual MS Indirect Costs
0	$5,771	$9,027
1	$9,920	$12,349
2	$14,070	$15,672
3	$18,217	$18,994
4	$22,365	$22,317
5	$26,515	$25,639
6	$30,664	$28,962
7	$34,812	$32,284
8	$38,960	$35,607
9	$43,109	$38,930

EDSS: Expanded Disability Status Scale, MS: multiple sclerosis

Key Model Inputs: Treatment Costs

Drug	WAC per Year	Net Price per Year	Source
Ublituximab	Year 1: $68,833 Years 2+: $59,000	Year 1: $53,260 Years 2+: $45,651	Redbook and assumption,* 6% mark-up not included
Natalizumab	$102,128	$100,902	Redbook and SSR Health, 6% mark-up not included
Ofatumumab	Year 1: $119,686 Years 2+: $89,760	Year 1: $87,730 Years 2+: $65,797	Redbook and SSR Health
Ocrelizumab	$71,187	$55,081	Redbook and manufacturer net price, 6% mark-up not included
Rituximab	Year 1: $6,229 Years 2+: $4,153	Year 1: $6,229 Years 2+: $4,153	Biosimilar rituximab average sales price, 6% mark-up not included
Dimethyl Fumarate	Year 1: $2,762 Years 2+: $2,739	Year 1: $2,762 Years 2+: $2,739	Redbook

WAC: wholesale acquisition cost
*23% discount assumed based on ocrelizumab

Results

Base-Case Results: Lifetime Model Outcomes

Treatment	Total Cost	QALYs	evLYs	Life Years	Years Without Ambulatory Restrictions*	Years Without a Wheelchair†
Ublituximab	$1,683,000‡	12.64	12.81	20.35	13.60	16.99
Natalizumab	$2,636,000	13.34	13.56	20.62	14.73	17.90
Ofatumumab	$1,960,000	12.57	12.73	20.32	13.48	16.89
Ocrelizumab	$1,829,000	13.89	14.13	20.82	15.61	18.56
Dimethyl Fumarate	$1,065,000	11.27	11.27	19.83	11.51	15.13

EDSS: Expanded Disability Status Scale, evLY: equal-value life year, QALY: quality-adjusted life year

*As measured by time in EDSS health states less than 5.

†As measured by time in EDSS health states less than 7.

‡Assuming a 23% WAC to net price discount.

Base-Case Incremental Results

Treatment	Cost per QALY Gained	Cost per evLY Gained	Cost per Life Year Gained	Cost per Additional Year without Ambulatory Restrictions*	Cost per Additional Year without a Wheelchair†
Ublituximab‡	$451,000	$403,000	$1,200,000	$295,000	$332,000
Natalizumab	$760,000	$687,000	$2,000,000	$487,000	$567,000
Ofatumumab	$690,000	$616,000	$1,800,000	$453,000	$508,000
Ocrelizumab	$292,000	$267,000	$771,000	$186,000	$223,000

EDSS: Expanded Disability Status Scale, evLY: equal-value life year, QALY: quality-adjusted life year

*As measured by time in EDSS health states less than 5.

†As measured by time in EDSS health states less than 7.

‡Assuming a 23% WAC to net price discount for cost of ublituximab.

Sensitivity Analyses

- One-way sensitivity analyses
  - Main driver is hazard ratio on disease progression for all interventions
    - For ublituximab, incremental cost-effectiveness ratios ranged from $130,000 per QALY to more costly, less effective
- Probabilistic sensitivity analyses
  - Majority of iterations above $200,000 per QALY/evLY for all interventions
    - For ublituximab, 0% less than $100,000 per evLY gained, 12% less than $150,000 per evLY gained, 26% less than $200,000 per evLY gained

Scenario Analyses

- Modified societal perspective
  - Incremental cost-effectiveness ratios became more favorable by 3-7%
  - Still above common cost-effectiveness thresholds
- Treatment stop after EDSS 7
  - Incremental cost-effectiveness ratios became more favorable by 3-9%
  - Still above common cost-effectiveness thresholds
- Monoclonal antibody biosimilar comparator
  - Ranged from far exceeding common thresholds to more costly, less effective

Health-Benefit Price Benchmarks

Intervention	Annual WAC	Annual Price at $100,000 Threshold	Annual Price at $150,000 Threshold	Discount from WAC to Reach Threshold Prices
Ublituximab	$59,000	$16,500	$34,900	41%-72%
Natalizumab	$102,128			66%-84%
Ofatumumab	$89,760			61%-82%
Ocrelizumab	$71,187			51%-77%

WAC: wholesale acquisition cost

Limitations

- Model structure is based on health states defined by EDSS, which has been critiqued in that later levels focus too much on physical disability
- Natural history studies used for progression rates are 10+ years old
- Variation exists in the reported quality of life utility scores for people with MS at high levels of EDSS
- Rituximab was not modeled as an intervention in the cost-effectiveness analysis due to insufficient evidence on disease progression

Comments Received

- Use quality of life values less than zero for EDSS 8 and 9
- Stop treatment once a patient has reached EDSS 7
- Apply trial-reported discontinuation for each model cycle

Conclusions

- At their estimated net prices, each intervention exceeds standard cost-effectiveness levels in the US health care system
- The cost-effectiveness findings are primarily driven by a treatment's ability to slow disability progression as well as the annualized net prices

Questions

Manufacturer Public Comment and Discussion

Melissa Hamilton, MPH, Executive Director, WW HEOR US Immunology, Bristol Myers Squibb

Conflicts of Interest:

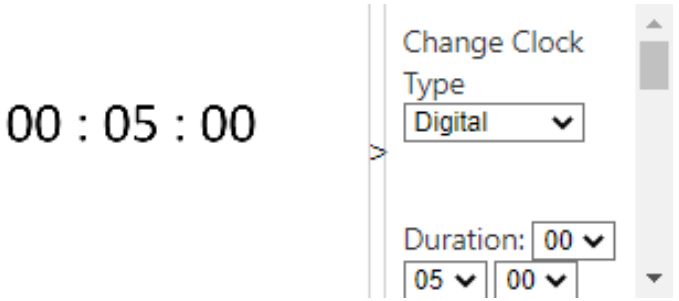
- *Melissa Hamilton is a full-time employee at Bristol Myers Squibb.*

00 : 05 : 00

Kyle Hvidsten, MPH, Head, Specialty Care, HEVA, Sanofi

Conflicts of Interest:

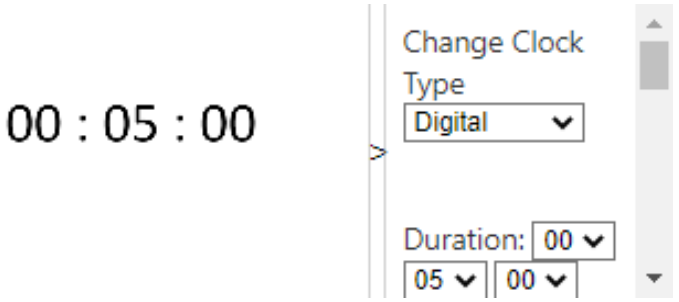
- *Kyle Hvidsten is a full-time employee at Sanofi.*



Ashish Pradhan, MD, Executive Director, Neuroimmunology, Genentech

Conflicts of Interest:

- *Dr. Ashish Pradhan is a full-time employee at Genentech.*



Public Comment and Discussion

Bari Talente, JD, President, MS Coalition; EVP, Advocacy and Healthcare Access, National MS Society

Conflicts of Interest:

- *No conflicts of interest to disclose.*

00 : 05 : 00

Lunch

Meeting will resume at 12:45pm ET

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Voting Questions

Patient Population for all questions:

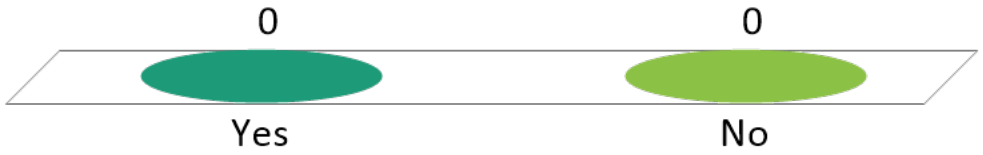
Adults with relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting multiple sclerosis, and active secondary-progressive multiple sclerosis.

Clinical Evidence

1. Given the currently available evidence, is the evidence adequate to distinguish the net health benefit provided by ublituximab from that provided by other monoclonal antibodies (natalizumab, ofatumumab, ocrelizumab, and rituximab)?

A. Yes

B. No



If yes, answer question 1a:

1a. For which of the following agents is the evidence adequate to demonstrate that the net health benefit of ublituximab is superior? (Select all that apply.)

A. Natalizumab

B. Ofatumumab

C. Ocrelizumab

D. Rituximab

2. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of ublitixumab is superior to that provided by fumarates (dimethyl fumarate, diroximel fumarate, and monomethyl fumarate)?

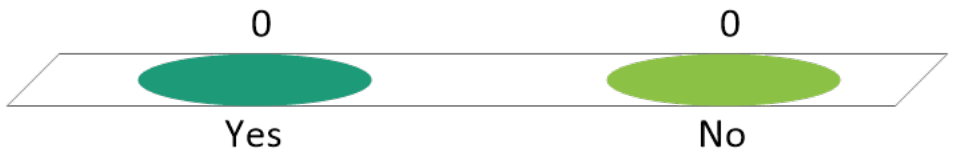
A. Yes

B. No

3. Given the currently available evidence, is the evidence adequate to demonstrate that the net health benefit of ublituximab is superior to that provided by fingolimod?

A. Yes

B. No



Contextual Considerations and Potential Other Benefits or Disadvantages

When making judgments of overall long-term value for money, what is the relative priority that should be given to any effective treatment for multiple sclerosis, on the basis of the following contextual considerations?

Acuity of need for treatment of individual patients based on short-term risk of death or progression to permanent disability

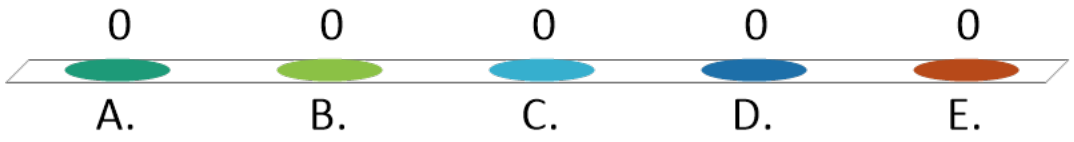
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



Magnitude of the lifetime impact on individual patients of the condition being treated

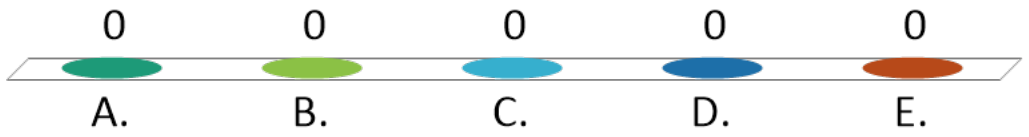
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



Other (as relevant)

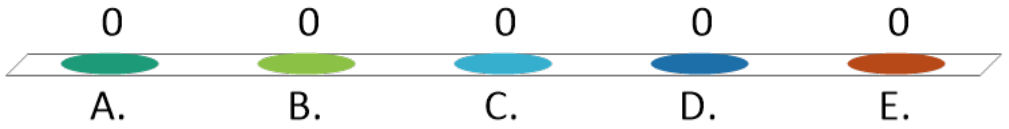
A. Very low priority

B. Low priority

C. Average priority

D. High priority

E. Very high priority



What are the relative effects of ublituximab versus dimethyl fumarate on the following outcomes that inform judgment of the overall long-term value for money of ublituximab?

Patients' ability to achieve major life goals related to education, work, or family life

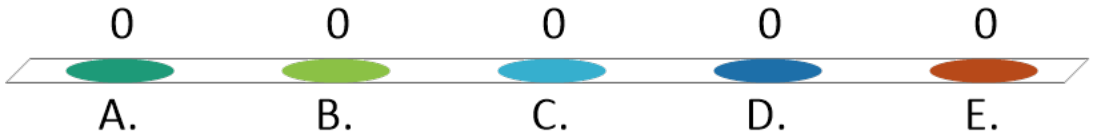
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



Caregivers' quality of life and/or ability to achieve major life goals related to education, work, or family life

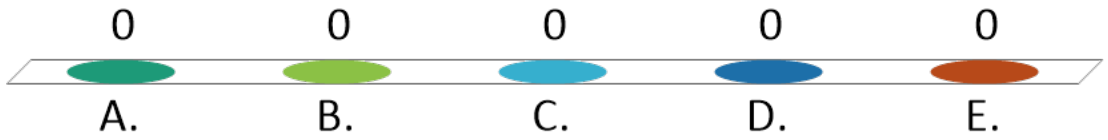
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



Society's goal of reducing health inequities

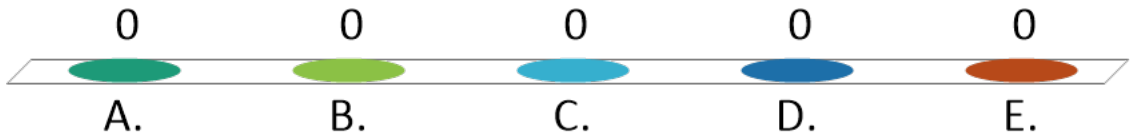
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



Other (as relevant)

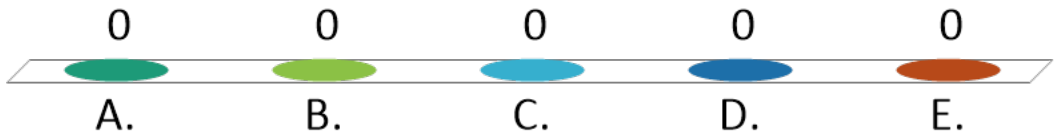
A. Major negative effect

B. Minor negative effect

C. No difference

D. Minor positive effect

E. Major positive effect



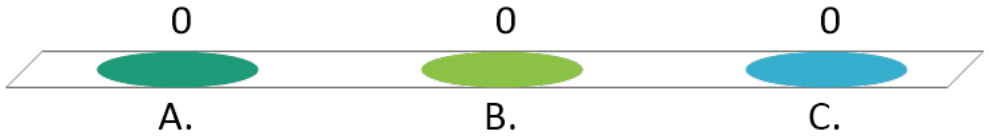
Long-Term Value for Money

8. Given the available evidence on comparative effectiveness and incremental cost effectiveness, and considering other benefits, disadvantages, and contextual considerations, what is the long-term value for money of treatment at current pricing with ublituximab versus dimethyl fumarate?

A. Low long-term value for money at current price

B. Intermediate long-term value for money at current price

C. High long-term value for money at current price



Break

Meeting will resume at 2:00 pm ET

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Policy Roundtable

Policy Roundtable

Policy Roundtable Participant	Conflict of Interest
Bruce Cohen, MD, Professor of Neurology, Northwestern Feinberg School of Medicine/Northwestern Medicine	Dr. Cohen has equity interests in Abbott Laboratories, AbbVie, and CVS Health. He also served as a site PI for the OPERA trial of ocrelizumab funded by Northwestern University.
David Dohan, MD, Medical Director, Pharmacy, Point32Health	Dr. Dohan is an employee at Point32Health.
Lauren Hirschfeld, Person Living with MS; District Activist Leader, National MS Society	No conflicts of interest to disclose.
Annette Langer-Gould, MD, PhD, Regional Lead, Translational Neuroscience, Southern California Permanente Medical Group	Dr. Langer-Gould served as the site PI for ocrelizumab in the relapsing-remitting Phase III trial. Dr. Langer-Gould also served as the Assistant Medical Director at Genentech from September 2006 – September 2007, where she oversaw the rituximab and ocrelizumab development programs.
William Rose, MBA, Executive Director, Access Marketing and Health Economics Outcomes Research, TG Therapeutics	William is an employee at TG Therapeutics.
Bari Talente, JD, Executive Vice President, Advocacy and Healthcare Access, National MS Society	No conflicts of interest to disclose.
Daniel Uting, PharmD, Senior Clinical Pharmacist, Utilization Management Strategy, Prime Therapeutics	Dr. Uting is an employee at Prime Therapeutics.

New England CEPAC Council Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around February 17, 2023
  - Includes description of New England CEPAC votes, deliberation, policy roundtable discussion
- Materials available at: https://icer.org/assessment/multiple-sclerosis-2023/#timeline

Adjourn

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Direct Evidence: ULTIMATE I & II

Outcomes		Trial			
		ULTIMATE I		ULTIMATE II	
		Ublituximab	Teriflunomide	Ublituximab	Teriflunomide
N		271	274	272	272
ARR	RR (95%CI); p-value	0.41 (0.27, 0.62); p<0.001		0.51 (0.33, 0.78); 0.002	
CDP-3	HR (95%CI); p-value	0.84 (0.5, 1.41); 0.51			
CDP-6	HR (95%CI)	0.66 (0.36, 1.21)			
NEDA	%	44.6%	15.0%	43.0%	11.4%
MSFC	mean change	0.47	0.27	0.52	0.28
Gd+ T1 Lesions	RR (95%CI); p-value	0.03 (0.02, 0.06); <0.001		0.04 (0.02, 0.06); <0.001	
New or Enlarging T2 lesions	RR (95%CI); p-value	0.08 (0.06, 0.10); <0.001		0.10 (0.07, 0.14); <0.001	